REMARKS

Applicants respectfully request reconsideration of the instant application in view of the foregoing amendments and the following remarks. Claims 46-55, 57 and 59-71 are pending in the application. Claims 50-51, 59-60, 66 and 67 have been amended to better track current business practices and implementations. Applicants maintain that the claims in their original form and in their prior pending form were in condition for allowance and explicitly reserve the right to return to those form(s) and argue patentability at a later time. Applicants submit that support for the Amendment may be found throughout the originally-filed specification and claims. As such, no new matter has been added by these amendments. Reconsideration of this application is respectfully requested.

Claim Objections

In the Office Action dated March 25, 2008, the Examiner objects to Claim 52 for "failing to further limit parent claim 51 because the Pro-PAP-S protein does not further limit SEQ ID NO:2 because the specification indicates that Pro-PAP-S cannot be other than SEQ ID NO:2." Examiner has also objected to Claims 50 and 60 for reciting "pro-PAP-S" and suggests that "a pro-PAP-S" protein be replaced with "SEQ ID No:2". Applicants respectfully disagree that the claim should be limited only to SEQ ID No: 2.

Regarding the examiners objection to Claim 50, Claim 50 has been amended to recite, "(i) a nucleic acid molecule encoding a pro-PAP-S or a C-terminal deletion thereof; and (ii) an inducible promoter which induces expression of said pro-PAP-S...wherein expression of said pro-PAP-S or C-terminal deletion thereof induces cell death in said specific cells of said plant". Claim 60 has been amended similarly. These amendments better track applicants current business practices.

The originally filed specification and claims supports these amendments. The originally filed specification states, "In accordance with a third aspect of the invention, the present invention provides a method of inducing a necrotic effect in specific cells of a plant, wherein the plant is transformed with a chimaeric gene, the coding sequence of said gene coding for a precursor PAP molecule or a C-terminal deletion thereof, said gene comprising a promoter with acts in response to the application of a specific stimulus to the plant, so that protein expressed by the coding sequence is expressed in specific cells of said plant, said promoter being appropriately selected to provide one of the following effects: nematode infection disruption, sterility, changes in flower morphology, abscission, seed release or trichome development." (p.17 line 22- p. 18, line 9 of original specification). Also see pg 18, line 17-20, "In respect of the third aspect the coding sequence preferably encodes one of the following list: the Pro-PAP-S, the nucleotide sequence being given in SEQ ID NO 1 and the amino acid sequence being given in SEQ ID No. 2, or PAP'...". In addition, see original claims 22-24.

The skilled person would have known at the filing date of the application which proteins are encompassed by the term "pro-PAP-S". For example, a complete cDNA encoding PAP-S has been isolated, sequenced and characterized (Poyet J-L. *et al.* (1997) *FEBS Lett* **406,** 97-100; see paragraph 3.1 and Figure 1). The deduced amino acid sequence for pro-PAP-S is provided in Figure 1 of that document and also in SEQ ID NO. 2 of the present application.

There is believed to be only one precursor to the mature PAP-S protein, although variants of this precursor do exist in nature and were known at the filing date of the application (see paragraph 3.1 of Poyet J-L. *et al.*). It is not, therefore, appropriate for claims 50 and 60 to be restricted to the sequence set forth in SEQ ID NO: 2, as the Examiner has requested.

Based on the amended claims and stated teachings in the application, the skilled person would also know which changes could be made to the amino acid sequence given

in SEQ ID NO: 2 without affecting the pro-enzyme properties of pro-PAP-S (see below for further discussion).

Accordingly, a person skilled in the art would be able to use the approach in amended claims 50-52 and 60.

Rejections under 35 USC § 112

Enablement

The Examiner has rejected independent claim 46 and dependent claims 61-62 and 70-71 on the ground that the specification does not reasonably provide enablement for a method of inducing cell death in any plant cells with a nucleic acid molecule encoding pokeweed antiviral protein having at least 70%, 80% or 90% homology to SEQ ID NO 2, 6, 8. Applicants respectfully disagree.

Claim 46 relates to "...a nucleic acid molecule encoding pokeweed antiviral protein wherein the protein is at least 70% homologous with a pokeweed antiviral protein selected from the group consisting of the pro-PAP-S protein of SEQ ID NO: 2, the PAP-S β protein of SEQ ID NO: 8, and the PAP-S α protein of SEQ ID NO: 6;...wherein said pokeweed antiviral protein induces cell death in said specific cells of said plant."

The Examiner has asserted that the specification does not teach which modifications may be made to the disclosed amino acid sequences in order to arrive at both the structural and functional limitations of the claim. Accordingly, the Examiner states, "one skilled in the art would have to make all possible nucleotide substitutions and deletions in SEQ ID NO: 1-2, 5-6, or 7-8 and test all sequences that meets the structural limitations to determine which also meet the functional limitation." (p. 5 Office Action dated March 25, 2008).

Applicants respectfully disagree. One skilled in the art would not have to make "all possible nucleotide substitutions and deletions" to the claimed sequences. It was known at the time of filing which amino acids in a PAP are essential for the induction of

cell death in a transformed plant, as the amino acids responsible for interacting with the ribosome and cleaving rRNA have been identified. For example, Chaddock J. A. *et al.* (1994) *Nucleic Acids Res* **22**,(9) 1536-1540 provides some examples of PAP mutations which abolish its ribosome-inactivating ability, so indicating amino acids that are essential for this function. Chaddock et al., also identifies the pro-sequence of pro-PAP (see Discussion p. 1538). Since the amino acid sequence of PAP-S is very similar to that of PAP (see paragraph 3.1 of Poyet J-L. *et al.*), mutations to PAP that affect its activity, such as those disclosed in Chaddock J. A. *et al.*, would be expected to have a similar effect on PAP-S. Thus, the skilled person would not have to make 'all possible' modifications to the sequences set forth in SEQ ID NOs. 2, 6 and 8 and test whether they retain the requisite function. Rather, the skilled person would know that only the non-essential amino acids could be modified without compromising the protein's activity.

The skilled person would thus know to modify only the non-essential amino acids. He would also be able to predict the conservative modifications that could be made such that the resultant protein maintained its tertiary and any quaternary structure. The skilled person would thus be able to synthesise nucleic acid molecules that code for a pro-enzyme which may be cleaved to produce active PAP-S or that code for the mature protein.

Furthermore, the specification enables a person of skill in the art to establish whether a given change in sequence has the function referred to in claim 46. Pages 38-39 of the application as filed describe an embodiment using a GUS reporter gene assay for detecting ribosome inactivation. A cell death assay could also be used to test whether a given amino acid sequence has the ability to induce cell death. The availability of such tests ensures that there is no undue burden placed on the skilled person when seeking to ascertain whether a given method falls within the scope of the claims. The throughput of such tests is sufficient for the skilled person to test the limited number of amino acid

sequences that he would generate in practice (as above) for the ability to induce cell death.

For the foregoing reasons, applicants submit that the claims are enabled and in condition for allowance.

Other Matters

Claims 50, 59 and 60 as on file refer to "a nucleic acid encoding a mature pokeweed antiviral protein... selected from the group consisting of a pro-PAP-S protein...". These claims have been amended to refer to "a nucleic acid encoding a pokeweed antiviral protein...selected from the group consisting of a pro-PAP-S protein..." to better tract current business practices and implementations. Applicants maintain that the claims in their original form and their prior pending form were in condition for allowance and explicitly reserve the right to return to those form(s) and argue patentability at a later time.

A typographical error in claims 66 and 67 has also been corrected.

Conclusions

In view of the above amendments and remarks, applicants respectfully submit that requirements under USC § 112 have been entirely fulfilled and the claims are in condition for allowance.

Consequently, the reference(s) cited and/or any official notice taken by the office action do not result in the claimed invention, there was/is no motivation for such a combination of references (i.e., cited references do not teach, read on, suggest, or result in the claimed invention(s)), and the claimed inventions are not admitted to be prior art. Thus, the Applicant respectfully submits that the supporting remarks and claimed inventions, claims 46-55, 57 and 59-71, all: overcome all rejections and/or objections as

noted in the office action, are patentable over and discriminated from the cited reference(s), and are in a condition for allowance. Furthermore, Applicant believes that the above remarks, which distinguish the claims over the cited reference(s), pertained only to noted claim element portions. These remarks are believed to be sufficient to overcome the prior art. While many other claim elements were not discussed, Applicant does not concede that any such elements are found in the prior art and/or within any official notice taken in the office action, and as such, Applicant asserts that all such remaining and not discussed claim elements, all, also are distinguished over the prior art, including any official notice taken in the office action, and explicitly reserves the opportunity to more particularly remark and distinguish such remaining claim elements at a later time should it become necessary. Further, any remarks that were made in response to an Examiner objection and/or rejection as to any one claim element, and which may have been re-asserted as applying to another Examiner objection and/or rejection as to any other claim element(s), any such re-assertion of remarks is not meant to imply that there is commonality about the structure, functionality, means, operation, and/or scope of any of the claim elements, and no such commonality is admitted as a consequence of any such re-assertion of remarks. As such, Applicant does not concede that any claim elements have been anticipated and/or rendered obvious by any of the cited reference(s). Accordingly, applicant respectfully requests allowance, and the reconsideration and withdrawal of the rejection(s) and/or objection(s).

In the event that a telephone conference would facilitate examination of the application in any way, the Examiner is invited to contact the undersigned at the number provided. Although Applicants believe that no additional extensions of time are necessary, should the Commissioner deem further extensions necessary, such extension is hereby petitioned for. Also, the Commissioner is hereby authorized to charge any fees which may be required to Deposit Account 03-1240, No. 17132-029US.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. 03-1240, Order No. 17132-029US. In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 03-1240, Order No. 17132-029US.

Respectfully submitted,
CHADBOURNE & PARKE , L.L.P.

Dated: August 25, 2008

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